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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/049,865	03/27/1998	COLLIN J. WEBER	47765/C/JPW/	6162

23914 7590 01/15/2002

STEPHEN B. DAVIS  
BRISTOL-MYERS SQUIBB COMPANY  
PATENT DEPARTMENT  
P O BOX 4000  
PRINCETON, NJ 08543-4000

EXAMINER

DAVIS, MINH TAM B

ART UNIT	PAPER NUMBER
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1642

DATE MAILED: 01/15/2002

24

Please find below and/or attached an Office communication concerning this application or proceeding.

**Advisory Action**

Application No.

09/049,865

Applicant(s)

WEBER ET AL.

Examiner

MINH-TAM DAVIS

Art Unit

1642

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 04 July 2001 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

**PERIOD FOR REPLY [check either a) or b)]**

- a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
- b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on \_\_\_\_\_. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☒ The proposed amendment(s) will not be entered because:
- (a) ☒ they raise new issues that would require further consideration and/or search (see NOTE below);
  - (b) ☒ they raise the issue of new matter (see Note below);
  - (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
  - (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: See attached.

3. ☐ Applicant's reply has overcome the following rejection(s): \_\_\_\_\_.
4. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. ☒ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: See attached.
6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. ☒ For purposes of Appeal, the proposed amendment(s) a) ☒ will not be entered or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: NONE.

Claim(s) objected to: NONE.

Claim(s) rejected: 1,2,4-7,9-14,16,17,20,23,43-47.

Claim(s) withdrawn from consideration: 48-64.

8. ☐ The proposed drawing correction filed on \_\_\_\_\_ is a) ☐ approved or b) ☐ disapproved by the Examiner.
9. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). \_\_\_\_\_.
10. ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

Effective February 7, 1998, the Group Art Unit location has been changed, and the examiner of the application has been changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Minh-Tam Davis, Group Art Unit 1642.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Applicant cancels claims 1, 2, 4-7, 9-14, 16, 17, 20, 23 and 43-47, and adds new claims 48-64.

New claims 48-64 have not been entered, because they introduce new matter (an immune system costimulation event mediated by CD4 in claim 48), and would require new search for 1) an immune system costimulation event mediated by a cell surface molecule selected from the group consisting of B7, CD28, CTLA4, GP39, CD40 and CD4, and 2) an agent which is GK1.5 or MR1, and 3) a semipermeable membrane which is double-walled.

### **REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, SCOPE**

Claims 1, 2, 4-7, 9-14, 16, 17, 20, 23 and 43-47 remain rejected under 35 USC 112, first paragraph, pertaining to lack of enablement for any agent which inhibits an immune system costimulation event, for reasons already of record in paper No.11 .

### **REJECTION UNDER 35 USC 103**

Claims 1, 2, 4-7, 9-14, 16, 17, 20, 23 and 43-47 remain rejected under 35 USC 103, pertaining to obviousness over Lenschow et al, in view of Goosen et al, Soon-Shiong et al, Akalin et al, Linsley et al, Padrid et al, and Steurer et al for reasons already of record in paper No.11.

Applicant argues that the results are unexpected. The graft survival with both CTLA4Ig and microencapsulation together is over 4- fold longer than with microencapsulation alone and over 20-fold longer than with CTLA4Ig alone. Nothing in the cited references would permit one to foresee such a dramatic increase.

Applicant's arguments set forth in paper No.12 have been considered but are not deemed to be persuasive for the following reasons:

One of ordinary skill in the art would have expected that the combination of CTLA4Ig and microencapsulation together would produce results, i.e. increasing the chance of preventing graft rejection, better than with microencapsulation alone or with CTLA4Ig alone, because CTLA4Ig and microencapsulation complement each other. That is CTLA4Ig inhibits T cell activation, cell-mediated and humoral immune response, prevents macrophage activation and infiltration into the graft site, and inhibits immunoglobulin secretion, as taught by Lenschow et al, Akalin et al, and Linsley et al, whereas microencapsulation is impermeable to immune system proteins, and protects the transplanted cells from both cytotoxic T-lymphocytes and natural killer cells, as taught by Goosen et al and Soon-Shiong et al.

Moreover, MPEP 2145 teaches that a mere recognition of additional advantages which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). MPEP 2145 further teaches that a mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention. *In re Wiseman*, 596 F.2d 1019, 201 USPQ 658 (CCPA 1979). Granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 703-305-2008. The examiner can normally be reached on 9:30AM-4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, ANTHONY CAPUTA can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.


Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0916.

Application/Control Number: 09/049,865  
Art Unit: 1642

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MINH TAM DAVIS

January 14, 2002

  
ANTHONY C. CAPUTA  
SUPERVISORY PATENT EXAMINER  
TECHNOLOGY CENTER 1600

**Attachment for PTO-948 (Rev. 03/01, or earlier)**  
**6/18/01**

**The below text replaces the pre-printed text under the heading, "Information on How to Effect Drawing Changes," on the back of the PTO-948 (Rev. 03/01, or earlier) form.**

**INFORMATION ON HOW TO EFFECT DRAWING CHANGES**

**1. Correction of Informalities – 37 CFR 1.85**

New corrected drawings must be filed with the changes incorporated therein. Identifying indicia, if provided, should include the title of the invention, inventor's name, and application number, or docket number (if any) if an application number has not been assigned to the application. If this information is provided, it must be placed on the front of each sheet and centered within the top margin. If corrected drawings are required in a Notice of Allowability (PTOL-37), the new drawings **MUST** be filed within the **THREE MONTH** shortened statutory period set for reply in the Notice of Allowability. Extensions of time may **NOT** be obtained under the provisions of 37 CFR 1.136(a) or (b) for filing the corrected drawings after the mailing of a Notice of Allowability. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

**2. Corrections other than Informalities Noted by Draftsperson on form PTO-948.**

All changes to the drawings, other than informalities noted by the Draftsperson, **MUST** be made in the same manner as above except that, normally, a highlighted (preferably red ink) sketch of the changes to be incorporated into the new drawings **MUST** be approved by the examiner before the application will be allowed. No changes will be permitted to be made, other than correction of informalities, unless the examiner has approved the proposed changes.

**Timing of Corrections**

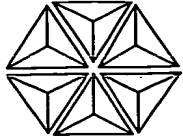
Applicant is required to submit the drawing corrections within the time period set in the attached Office communication. See 37 CFR 1.85(a).

Failure to take corrective action within the set period will result in **ABANDONMENT** of the application.

**RECEIVED**

NOV 05 2002

OFFICE OF PETITIONS



**Bristol-Myers Squibb Company**

**Worldwide Medicines Group**

**P.O. Box 4000 Princeton, NJ 08543-4000**  
**609 252-3953 Fax: 609-252-4526**

**TO:** Alan J. Morrison, Cooper & Dunham  
Shirley A. Vanier, Emory University  
**FROM:** Christopher A. Klein, Counsel, Biotechnology Patents  
**DATE:** February 4, 2002  
**RE:** USSN 09/049,865, "Method of Inhibiting Immune System Destruction of  
Transplanted Viable Cells"  
Our Docket No. ON0128B  
Your Docket No. 47765-C

***PRIVILEGED AND CONFIDENTIAL***  
***ATTORNEY-CLIENT COMMUNICATION***

THIS COMMUNICATION CONCERNS THE ABOVE-IDENTIFIED CASE  
ATTACHED PLEASE FIND A COPY OF Office Action DATED 1/15/02, WHICH WE  
RECEIVED FROM U.S. Patent Office

PLEASE NOTE THAT A RESPONSE IS DUE

WE ARE SENDING THIS FORM FOR THE FOLLOWING REASON(S):

☒ FOR YOUR INFORMATION

☐ PLEASE REVIEW AND CONTACT US PRIOR TO TAKING ACTION

☐ PLEASE TAKE THE FOLLOWING ACTION:

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☐ NO ACTION IS REQUIRED BY YOUR OFFICE

☐ COMMENTS:

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